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AUTHOR McClain, William A.; Jerman, George
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ABSTRACT

Reviewed on a layman's level was research on psychopharmacology with the emotionally and behaviorally disturbed. General conclusions drawn from the man y studies were that the effect of drugs on intellectual functioning had not been determined and that there was little evidence to indicate that the learning process was consistently and reliably affected in certain predictable ways. It was advised that the psychologist be informed when a subject was receiving drug medication, the drug name, and dosage. The review concerned stimulants, tranquilizers, and sedatives frequently used by pediatricians. Stimulants referred to in research included dextroamphetamine, D-amphetamine, methylphenidate, monoaminoxidase inhibitors, amitriptyline, proamitriptyline, and cholinergics; methylphenidate was the drug used most often. Tranquilizers cited were thioridazine, chlorpromazine, reserpine, phenothiazines, diphenylmethanes, fluphenazine hydrochloride, chlorprothixene hydrochloride, primazine hydrochloride, and thi rpropazate; drugs were found to be an advisable treatment for behaviorally disordered children. Sedatives covered included diphenylhydantoin sodium and captodiamine hydrochloride. (CB)

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PSYCHOPHARMACOLOGY WITH THE BEHAVIORALLY DISTURBED: A REVIEW

William A. McClain, Ph.D.
Counseling Psychologist
D. C. Children's Center
Laurel, Maryland 20810

George Jerman, M.Ed.
School Psychologist
Howard County Board of Education
Clarksville, Maryland

EC 041 702

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INTRODUCTION

Treatment for behaviorally disordered children can be separated into three general categories: psychotherapy, milieu or environmental therapy, and chemotherapy. It is this latter group that is explored in this paper.

The paper originated from the writers' interest over the increasing number of children found in both the public schools and institutions who were receiving or had recently been receiving some kind of internal medication of a drug form. Many reasons could be offered to account for this state of affairs. Several of the more important ones include:

1. Overabundance of complimentary samples supplied to physicians by pharmaceutical houses make prescription of same a very convenient choice.

2. Shortages of mental health workers, adequate programs, and child specialists have created "time" premiums and priorities. In short, when case loads become excessively large, and the demand for long or short term therapy, although needed, cannot be provided, chemotherapy is sometimes used as a "better than nothing" technique. Frequently, too, prescribers of drugs are not fully cognizant of the emotional referents underlying a problem. What occurs is treatment of the major physical

symptom(s), at the expense of neglecting the true emotional pathology underlying the symptom(s).

3. Psychological predispositions and dependencies existing in our culture that aim for instantaneous and impulsive cures. Where traditional therapies may require a large number of sessions before progress becomes overtly visible, in addition to the well known phenomena of a patient characteristically becoming worse before getting better, the use of drugs, in contradistinction, typically creates an immediate diminuation of symptoms. This occurrence becomes a reinforcer for teachers, parents, and the doctor such that when success in drug therapy is found for one student or child there are often heard clamors for its dissemination to other students and children, frequently irrespective of different behavior problems. The press, as reflected by recent articles in popular news periodicals, and the television media to a lesser extent have, in many instances, popularized to their respective audiences the "miracle results" of certain drugs in remediating behavior problems. Likewise, a psychological set to take medication when "sick" is part and parcel of American tradition.

These factors are not meant in any way to be an exhaustive or mutually exclusive list, but rather serve as a starting point for highlighting the need for child specialists to add

to their professional armamentarium of skills. Nor are the writers questioning the legitimacy of such prescriptions after careful study of the problem, other alternatives, and in consultation with a professional team. Rather, emphasis is placed on suggesting that if drug therapy continues to increase in popularity as the treatment of choice, then definite implications emerge for the role and function of the psychologist. In short, he will need to be minimally conversant in the basic terminology of psychopharmacology, and to some degree be able to assess the anticipated effects, purposes, advantages and disadvantages of a particular drug in relation to the learning process. This dissemination of factual information and consultation may occur with a physician, a teacher, and/or parent. As a member of a psychological services team he may on occasion even initiate referrals for possible drug therapy, or suggest other, more efficient alternatives in its place.

Review of the available research did produce a number of sources that described the drugs and their observed effects that are in present use for treating disturbed and socially disordered youngsters. Although far short of a comprehensive review of chemotherapeutic agents for psychiatric disorders, a number of studies are reported that deal with many of the drugs that are in regular pediatric usage and that have been encountered frequently by the writers.

This review is organized in the three general drug classes: stimulants, tranquilizers, and sedatives. It appears that this arrangement give greatest consideration to presenting studies in an order that allows some comparison of their respective behavioral effects. The drugs have been referred to by their generic or chemical names in this treatment. To facilitate brand name associations and to encourage continued reference to this work, a table is included that lists the generic name alphabetically according to general drug groups. This name is followed by the better known brand or trade name of the drug. All efforts have been made to reduce the technical aspects of this scientific field to a minimum so that drug therapy can be understood on a fairly basic level. For this reason little mention is made of physiological or anatomical effects. Certainly the behavioral elements give us enough concern to warrant centering this investigation there.

STIMULANTS

It has been known for some years that stimulant drugs, such as dextroamphetamine, may have a beneficial effect on school performance of hyperkinetic or emotionally disturbed children (Bradley, 1937). Children treated with these stimulants rarely become excited, but rather tend to become more calm, purposeful, and organized in their behavior. In some children the alteration in behavior has been described as truly remarkable. Side effects -- other than mild anorexia and insomnia -- are rare, and these tend to diminish in most children, even with high dosage of the medication (Bradley, 1951; Bradley, 1958).

A recent study appears to lend strong support to claims that this drug action has its main behavioral effect on increasing drive level and response vigor in children. Fifty-eight children from a public school system, who had been selected by teachers as having serious learning problems, were randomly assigned to two groups. One group received a daily treatment of dextroamphetamine, the other a matched placebo for one month. At the end of this time, the treatments were switched. All treatments were double-blind. Measures of intellectual performance and assertiveness were obtained by objective, factor analyzed test measures. Teachers also rated

the children before and after each treatment. The results indicated that improved school performance and classroom behavior was substantial, but the objective test changes were questionable (Connors et.al., 1967).

Solomons (1965) has discussed some additional changes produced by dextroamphetamine therapy and cites loss of appetite, restlessness and interference with sleep activity, pale and sallow facial appearances, and nervousness after certain kinds of activities.

Zrull et.al., (1963) compared D-Amphetamine with other drugs. Sixteen children ages 7 to 14 of overall average intelligence received three medications in a double-blind, cross-over pattern for an eight-week period. A battery of tests, ratings by parents and teachers and medical people, and laboratory findings of physical changes were analyzed. Considerable improvements in all children were noted and continued to sustain in some children. The D-Amphetamine was judged more effective than chlordiazepoxide in the reduction of manifestations of the hyperkinetic syndrome. Both drugs appeared to be significantly more effective than the placebo.

Amphetamines have also been successfully used at times in modifying hyperactive behavior. They have been in use for many years (since approximately 1930) in the treatment of brain damage behavior symptoms (Bradley, 1958; Denhoff, 1961;

Laufer, et.al., 1937). This stimulant or activator drug has a similar paradoxical effect in seeming to calm and organize behavior in some children by reducing fluctuations in vigilance and alertness and increasing attention span (Bradley, 1951; Paine, 1962).

Other investigators have found amphetamines expecially helpful in cases of dyslexia where there is a short attention span or distractibility but no hyperactivity (Clements and Peters, 1962). Teachers reported that the child "seemed more interested in his work," or "at least had begun to show some progress in reading." The drug was administered at breakfast and at lunch and two forms of amphetamine sulfate were used. These authors maintain that racemic amphetamine sulfate acted differently from dextroamphetamine and was superior in its effect on some children.

A study by Laufer et.al. (1937) produced a significant improvement in the "hyperkinetically impulse disordered child" when treated with amphetamines and followed over a three-year period. In this study, attention span, hyperactivity, and behavioral ratings by teachers and neighbors could be manipulated in a positive way by increasing and decreasing dosages. Other investigators do not confirm these findings although it should be noted that they used only 20 mg. per day as a total dosage compared to Laufer's use of up to 40 mg. per day (Bender & Nightern, 1956, Fish, 1960, Freedman, 1958).

It has been suggested that the amphetamines act to alter organic or maturational impairments of brain functioning, but this hypothesis has not been supported by EEG changes accompanying behavioral improvements following drug administration (Lindsley & Henry, 1942).

Clement et.al. (1970) in a recent article articulated many of the abuses of amphetamine and amphetamine-like drugs. It was noted that these drugs possess a wide variety of undesirable side effects even at recommended dosage levels. Specifically, the authors stated:

> Instead of alertness, or wakefulness, the patient may complain of nervousness, insomnia, headache, irritability, and excessively increased motor activity. The peripheral adrenergic effects may cause blurred vision, excessively dilated pupils with photosensitivity, too rapid a heart rate, palpitations, cardiac arrhythmias, and hypertension. The patient often complains of a very dry mouth. Nausea and vomiting, diarrhea, or constipation may all occur. Difficulty in urinating may be due to interference with bladder sphincter control (P. 13 as appeared in Mental Health Digest, 1970, 2).

The authors go on to conclude that these complications have been responsible for the gradual decrease in therapeutic indications for the amphetamines in favor of safer drugs with fewer side effects. To further quote from the article, the authors state that amphetamines are "now indicated in a few rare conditions (Narcolepsy, and some hyperactive brain-damaged children)." The increasing awareness of the dangers of amphetamines was reflected from the market. The British government, for example, cut off methedrine supplies to all

physicians, dentists, and chemists with hospitals given a one year's grace.

Another alerting drug, methylphenidate, at dosages of up to 80 to 100 mg. per day, has been reported to have similar beneficial effects (Knobel, et.al., 1959). In a well-controlled study by Conners and Eisenberg (1963) significant improvement in behavior, learning, and maze performance was demonstrated in a group of emotionally disturbed children following a ten-day period of treatment with methylphenidate. These investigators commented on the wide individual variation in responsiveness among their patients. They cautioned that the practical or clinical value of a drug must be determined in groups of carefully selected patients, and further studies of the personality and other factors influencing responsiveness to the drug are needed before it can be clinically recommended. Another short term controlled study of 30 children with hyperactivity and signs of minimal brain dysfunction has shown that small but measurable improvements attributable to methylphenidate may be expected in tests of general intelligence and visual-motor perception (Millichap, et.al., 1968).

Knights and Hinton (1969) found that methylphenidate apparently improves the attention span of children with behavior and learning disorders. In a double-blind study of

40 children with minimal brain dysfunction using placebo controls over a six-week period, the authors found that both parents and teachers rated the children as being less distractible and more attentive when receiving the drug therapy. The improvement in motor control was considered to be secondary to the improved attention span.

Sprague, Barnes, and Werry (1970) evaluated the effects of methylphenidate in comparison to thioridazine (a tranquilizer) on the behavior of emotionally disturbed, underacheiving boys with a mean age of 94.2 months, and a mean IQ of 98.6. Three dependent measures -- learning (a one-trial learning task), reaction time, and activity level -- were taken in a highly structured laboratory situation. It was found using both laboratory and clinical measures that methylphenidate improved learning performance, while thioridazine decreased learning performance. Also with the improvement in performance, methylphenidate reduced activity. Their findings indicate methylphenidate improved attention. The classroom behavior observation measures corroborated the findings from the laboratory in that methylphenidate increased attention to school work and improved the quality of the child's behavior that day as rated by the teacher.

Despite the numerous clinical reports on the beneficial response to central nervous system stimulants, controlled

studies are limited and there is little satisfactory explanation of the mechanism by which these drugs act. Also, reports are conflicting as to the type of behaviorally disordered child likely to respond favorably. Many investigators consider the central nervous system stimulants are particularly effective in patients with an organic condition but that hyperkinesis attributed to emotional disorder is unresponsive to this therapy (Conrad & Insel, 1967).

A few studies have been discovered that use the drugs commonly classed as monoaminoxidase inhibitors. Freedman (1958) administered iproniazid to a group of autistic schizophrenic children and reported increased awareness of their surroundings and a greater use of language in some. Bender and Faretra (1961) stated that imipramine and the monoaminoxidase inhibitors seem promising in withdrawn, depressed adolescents and autistic children. Fish (1960) in a review of drug therapy in children's behavior disorders stated that the effectiveness of the anti-depressants has not yet been established in these situations. In their study of suicidal attempts in children, Lawler et.al. (1963) reported using imipramine and other anti-depressant drugs in some of their patients but did not give sufficient data to draw any positive conclusions. A different use of imipramine was reported by MacLean (1960) who found it

effective in the treatment of enuresis in children.

A controlled study by Lucas et.al. (1965) was undertaken to evaluate amitriptyline effects on a group of symptoms relating to depression in children. Fourteen children and adolescents were selected from a residential treatment center population and administered the drug in a placebo controlled double-blind study. The subjects were of various neurotic and psychotic diagnoses and ranged in age from 10 to 17. Behavioral changes were rated daily on a four point scale in nine categories. Of the ten patients completing this study, six showed significant improvement by needing fewer external controls or by responding better to controls while receiving the active drug. Two patients needed more control or responded more poorly to controls. Three of the ten patients showed a diminution in the frequency of somatic complaint and two patients participated more easily in activities while one became worse in this category. Peer relationships were rated significantly improved in only two patients. The drug, however, did not appear to diminish severe anxiety or serious acting-out behavior. It was concluded that this drug may be useful in certain carefully selected depressed children but must be considered as only part of a total treatment program.

Krakowski (1964) reports a pilot study with amitriptyline involving 122 randomly selected patients ranging from 2 to 18 years representing various diagnostic categories with behavioral disorders in predominance referred to a child guidance clinic. Varying amitriptyline dosages were administered from 1 to 12 months with observational reports made every week. Habit and conduct disorders appeared to diminish significantly and anxiety and acting-out symptoms as well as some neurotic traits seemed to decrease although there was a confusion with another treatment (psychotherapy) that some chronic neurotics and schizophrenic children were receiving. The same author, however, duplicated the pilot study with a double-blind cross-over controlled study providing a medicated period of 4 to 16 weeks (Krakowski, 1965). Overall satisfactory responses were obtained during drug treatment that was not obtained during the placebo period. The investigator concluded that the study confirmed the results obtained previously during the pilot study and showed amitriptyline to be a safe, active and effective agent markedly reducing symptoms in emotionally disturbed hyperkinetic children when applied as part of a therapeutic approach used in a child guidance clinic.

Kraft et.al. (1966) reports on the use of amitriptyline with 123 children who presented a variety of behavioral and

other disorders. The subjects included 103 boys and 20 girls ranging in age from 2 to 14 who were seen in a child psychiatric clinic and treated on an out-patient basis. The dosage ranged from 30 mg. to 80 mg. daily. The patients' progress was followed closely by phone during the administration of the medication. The overall results were interpreted by the investigators as "promising" since 60 percent of the 123 patients showed improvement as determined by clinical study. This led to the suggestion that physicians consider the drug as a useful agent in treating children with adjustment reactions of childhood and those with maturational brain dysfunction.

Nineteen briefs of research studies of foreign and domestic origin supplied by a pharmaceutical house (Dr. Richard T. Smith, Merck, Sharp and Dohme, Professional Information Consultant) showed 11 studies to favor amitriptyline and proamitriptyline, a derivative of the former, as therapy for enuresis. Most of these studies showed accompanying anti-depressant outcomes of positive value. However, three of the studies were conducted with elderly or adult patients as subjects and one study used severely retarded children. The general interpretation seems to be that these drugs can be tried under medical supervision but that drastic side effects might be expected.

One study was found dealing with another drug group, the cholinergics. The effect of deanol on the problem solving and emotional behavior of 42 children between the ages of 6 and 13 was investigated. Both medical and psychological appraisals were used to diagnose central nervous system or behavior disorders. A cross-over, double-blind experimental design was used, with the drug being administered in a dosage of 100 mg. daily. The drugs did not produce significantly different scores on the measures employed, over the scores obtained during placebo treatment. Side effects were non-existing (Kugel & Alexander, 1963).

The data collected and reviewed indicated that methylphenidate is the stimulant drug of choice and that the amphetamines were second in most reported success (Connors & Eisenberg, 1963; Millichap & Fowler, 1967). It is probably fair to say, however, that the use of most of these drugs for behavior disturbances in children with brain damage has rarely been shown to be a completely successful venture unless other medication is administered. Central nervous system stimulants appear to be the agents of choice but further research efforts are necessary before adequate results can be obtained.

TRANQUILIZERS

Some of these drugs have long been used as anti-anxiety and anti-psychotic agents. Although they can be divided on the basis of chemical structure into many main groups, the derivatives of the phenothiazine compound appear to be most useful in the therapy of the behaviorally disordered child (Kraft & Battin, 1969). Phenothiazines appear very effective in severely disturbed children with "primary behavior disorders" and organic schizophrenic disease (Fish, 1960). Extreme caution is encouraged, however, because of unexpected and erratic behavioral changes (Schiele & Benson, 1962).

Thioridazine has been mentioned as an effective medication in regard to various childhood difficulties such as epilepsy, mental retardation, perceptual disorders, and emotional disturbance (Zarling & Hogan, 1960). In addition, EEG studies have shown significant differences in the response of groups receiving treatment by thioridazine and/or a combination of this drug with diphenylhydantoin, a sedative (Boelhouwer, et.al., 1968; Ingram, 1964). These authors attempted to examine the diagnostic and therapeutic relationship of certain EEG patterns and behavioral disorders. The drug appeared to have a positive effect on both the abnormal EEG pattern and the incidence of behavioral problems.

Additional drugs including chlorpromazine and reserpine, a rau wolfia alkaloid, were also studied but it was concluded that the significance of these effects were not determined and that further studies of the chronic effect of these drugs on electroencephalographic patterns should be completed (Hollister & Barthel, 1959). The rau wolfia alkaloids are drugs that have less reliable action and are generally reserved for severe schizophrenic disorders which do not respond to phenothiazines. These drugs appear to be much less potent than the phenothiazines, but often produce serious side effects when given in large dosages (Fish, 1963).

Some evidence is existing to show that thioridazine is of benefit in the treatment of patients with mental retardation. LeVann (1961) investigated a group of 97 institutionalized children, comprised of retarded as well as emotionally disturbed cases with adequate intelligence. No side effects, the principal concern of this study, were observed. The writers determined that thioridazine has control over a wide variety of abnormal behavioral patterns in children. They further concluded that medication could be discontinued because the drug aided in breaking the continuum of symptoms and made the children more accessible for other treatment techniques. There appeared to be little difference of effects with retarded or children of average intelligence.

Badham and his associates (1963) treated both child and adult mental deficients with thioridazine and found it to be effective in controlling behavior disorders in a significant proportion of the patients. They felt this drug was particularly useful with subnormal children.

A smaller but better controlled study essentially produced the same results but the authors noted a significant difference between the level of measured intelligence and response to the drug (Allen et.al., 1963). Children who were moderately and mildly retarded responded significantly better to the use of the drug. Very seriously retarded children did not respond as well.

An evaluation of thioridazine in a series of 141 familial and organic mentally retarded patients ranging in age from 6 to 60 showed the drug to effect improvement throughout the I.Q. level in 54% and marked improvement in an additional 34% of the patients (Abbott et.al., 1965). Hyperactivity, temper tantrums, and self abuse were the symptoms most favorably decreased. There was a relative absence of undesirable drug effects and the effect on behavior encouraged the investigators to suggest thioridazine as a means of facilitating home management of the mentally retarded child so as to avoid commitment to an institution. This same intent was discussed by two medical doctors in their article concerned

with the office management of behavioral disorders (Oettinger & Simonds, 1962). Their presentation of a descriptive study of their use of the drug in medical practice led them to conclude that thioridazine is successful in treating the hyperkinetic behavior problems associated with seizures. They determined that the drug can be faithfully used in pediatric office practice, and will substantially broaden the effective limits of the pediatrician in dealing with children's behavior problems. These conclusions were supported by the findings of a survey of pediatricians in Canada (Doyle, et.al., 1969).

Connors & Eisenberg (1963) report that thioridazine has been valuable in the management of severely retarded individuals in a 1,250 bed institution. Seventy-two percent of the patients receiving the drug were judged to be greatly improved because of the reduction in aggressiveness, hyperactivity, and temper tantrums. Many patients thereby were able to derive greater benefits from the training and other therapeutic programs. The absence of side effects was a noticeable outcome of this drug therapy.

Other literature has shown similar beneficial outcomes. Sandison, et.al., (1960) used four investigative groups including a placebo group and found that only thioridazine gave significant improvement. Hollister and MacDonald (1959),

employing other phenothiazines as active controls, concluded that thioridazine was an active drug with advantages over the other phenothiazines. Ostfeld (1959) reported that over two-thirds of 117 patients were improved when studied under blind placebo cross-over design conditions. He also felt that thioridazine was the least toxic of the phenothiazines. These conclusions were confirmed by Fleeson, et.al., (1958).

A recent double-blind cross-over study undertook to examine the effects of thioridazine and methylphenidate, a stimulant; and a placebo in nine severely retarded males (Davis, et.al., 1969). Thioridazine significantly decreased stereotyped behavior without affecting non-stereotyped behavior. The effect of this drug in the present study lends support to the theory that characterized behavioral arousal as a cause of stereotypy rather than its result.

With regard to the use of thioridazine in epileptics, it should be noted that the phenothiazines have frequently been suspected of being capable of reducing seizure threshold in susceptible subjects. For this reason, it has been considered pertinent to attempt to prevent increase in seizure patterns by withholding the use of these drugs wherever possible and by recommending that anti-seizure medication be continued (Millichap & Fowler, 1967). A previously cited study indicated a reduction in seizure threshold on the

administration of this drug and while the number of cases exhibiting this is extremely small, this led to the recommendation that anti-convulsant medication be maintained or instituted in patients exhibiting overt seizures or suspected of latent epilepsy respectively if thioridazine is to be employed (Hollister & Barthel, 1959).

Experimental studies exploring the effects of phenothiazines on human EEG's have been numerous and quite varied and indicate that alteration of the EGG may take one of two forms. The tranquilizing properties of the phenothiazine appear to be manifest as an effect on the EEG resembling that of light drowsiness from which the subject could be easily aroused. A finding of increased synchronization and normalization of the EEG has been interpreted as indicative of a slight depressant action on the reticular activating system (Itil, et.al., 1967).

A paper by Pauig, et.al. (1961) is particularly interesting because of the attention it devotes to the incidents of epileptic seizures where thioridazine was used for treatment of behavior disorders in such patients. The conclusion was reached that the control of behavior disorders obtained with thioridazine also has a salutary effect on the convulsions previously experienced by the patient but it is important to note that anti-convulsant medication was maintained throughout. It was determined that this protects

the patient against seizures and that combination therapy has greater potential for total rehabilitation of epileptic patients that seizure control therapy only.

Frain (1960) evaluated the use of thioridazine in severely disturbed epileptics with psychoses. Using a group of 70 white females, this investigator charted changes in physiological and psychological behavior during a tranquilizer period, a period of treatment with chlorpromazine, and a treatment period with thioridazine. Physiological symptoms were decreased and positive personality traits were significantly increased during the thioridazine treatment period.

Paulson and Buffaloe (1964) summed up the findings of the previous study when they concluded that ". . .the lack of any apparent epileptogenic effect for more patients appears to make thioridazine a reasonable choice when a tranquilizer is needed for the patient with a seizure tendency." Unfortunately, most of the studies mask the presence of latent activity, as would appear to be the case in some patients exhibiting seizures following the institution of a phenothiazine.

Rinsley (1963) studied 20 adolescent psychiatric in-patients receiving 100 to 800 mg. of thioridazine daily for a two-year period. He concluded that the low incidence of side effects and the great improvement in interactive

relationships with peers and therapeutic staff justified the drug agent as highly effective for this population.

Statistical analysis of the data from a study by Itil et.al. (1967) reveals significant correlation between behavior alterations and EEG changes, both qualitatively and quantitatively. Twenty behaviorally disturbed children and adolescents with abnormal EEG's were treated with a combination of the diphenylhydantoin and thioridazine. Behavior was rated before and three months after drug treatment. EEG recordings were carried out at the same time behavior ratings were done. Three months after treatment, fifteen patients showed moderate to marked improvement, and fourteen of them were discharged. Although only a pilot study, it does substantiate previous findings that indicate that behavioral disorders and EEG patterns are linked.

In appears in recent years that the use of a major tranquilizer, thioridazine, in childhood behavior disorders has been extensively investigated. As a result, this drug has been recommended as an effective agent with a minimal incidence of side effects. It is apparent from this overview that this drug can be considered to be in continued use by a number of medical people in maintaining control with a number of behaviorally disordered children, but its effect on what occurs in the classroom and as a result of educational intervention need not be of primary concern.

Studies concerning some of the minor tranquilizers have also been reviewed and it is found that these drugs are primarily useful in mild to moderately severe neurotic and "primary behavior disorders" (Fish, 1963). Prepuberty children do not appear to become addicted or "drug regulated." Children with moderately severe and schizophrenic reactions are frequently helped by these medications (Fish, 1960). Trifluoperazine is reported as having extra strong stimulatory effects on severely withdrawn and autistic children (Fish, 1963). However, Smith (1965) finds that this drug given in doses ranging from 1 mg. to 15 mg. daily brought varying degrees of improvement to 30 of 38 emotionally disturbed children. All 38 of the patients were considered moderate to severe behavior problems, expressed in hyperactivity, aggressiveness, insomnia, nightmares, and sometimes bedwetting. Therapy with trifluoperazine helps make these children receptive to counseling and other supportive measures; schooling, work therapy, and interpersonal relations. Chlordiazepoxide, another phenothiazine, has been favorably compared to some of the better known chemotherapeutic agents but some studies have indicated that this drug has adverse excitatory effects (Fish, 1969; Zrull et.al., 1963).

The diphenylmethanes, another minor tranquilizing drug group, also are used in therapy for children. Diphenyl-hydramine has been used successfully for over a ten-year

period to treat behaviorally disordered and emotionally disturbed children (Denhoff, 1961; Fish, 1960). This drug has been found most useful in behavior disorders associated with hyperactivity, to reduce anxiety in very young children who are not hyperactive, and helpful in controlling moderate schizophrenic disorders. Little side effects other than fatigue have been found. Therefore, it is used also as a bedtime sedative (Fish, 1960). Hydroxyzine and azacyclonol are similar compounds but appear to be slower acting and weaker in effects (Fish, 1963). Meprobamate, a propanediol, is reported as effective with neurotic and behavior disorders including those associated with mild organic brain disease (Bender & Nightern, 1956). It appears less effective for hyperactive syndromes than the diphenylmethanes (Fish, 1963).

A recent review of additional anti-anxiety and anti-psychotic agents included fluphenazine hydrochloride and chlorprothixene hydrochloride, promazine hydrochloride and thiorpropazate. These drugs were tried on too few patients for adequate appraisal, however (Millichap & Fowler, 1967).

It appears quite apparent that the use of these drugs in therapy for the behaviorally disordered child is widespread. Pediatric and clinical practice as well as pharmaceutical research has more than adequately indicated the advisability of drug therapy with many types of behavior problems.

SEDATIVES

The use of sedatives or anti-convulsant medication in children with seizures of any variety, with or without behavioral symptoms, is usually mandatory. In such cases the aim of therapy is seizure control. The main rationale for such therapy is the prevention of the possible organic cerebral deterioration that repeated episodes of anoxia and possible head trauma may cause the patient with uncontrolled epilepsy. The effects of drug control of seizures on the interictal behavior disorders may vary, however. This behavior may worsen, improve, or remain unchanged (Glaser & Dixon, 1956). In general, diphenylhydantoin and primidone are the drugs of choice in psychomotor seizures (Pincus & Glaser, 1966). Phenobarbital often seems to lead to exacerbation of behavioral symptoms although it may be an effective anti-convulsant. Barbituates have been found to increase anxiety and disorganization in severely disturbed children (Fish, 1960).

The place of anti-convulsants in the treatment of children with behavior disorders and abnormal electroencephalograms who have no seizures is less certain. Early studies gave good evidence for use of diphenylhydantoin sodium compounds in the treatment of children whose behavior disorders were not associated with specific EEG abnormalities (Lindsley &

Henry, 1942; Walker & Kirkpatrick, 1947). Later treatments of the use of this sedative do not confirm the earlier findings, however (Fish, 1963; Freeman, 1966).

Green (1961) studied the effect of anti-convulsants on non-epileptic children with behavior disorders associated with a focal electroencephalographic abnormality. Of five children with hyperactivity, short attention span, and intellectual deficits, two were unchanged, two were "less hyperactive," and one "related better." In three others of normal intelligence who had varied behavioral problems, two improved their ability to concentrate and to relate to others. These unimpressive qualitative results are the general experience, and the use of anti-convulsants to modify behaviors in such cases is usually unsuccessful.

Reports of the efficacy of anti-convulsants in the control of hyperactivity are likewise limited and are concerned primarily with trials in children whose behavior and learning problems are complicated by convulsive seizures. Primidone, found effective in 7 of 10 patients in one study, has been recommended for use in children with major convulsions and hyperactive behavior (Millichap & Fowler, 1967). Diphenylhydantoin sodium was relatively ineffective in two studies that included a total of only 28 patients, but the necessity for further trial is suggested by laboratory

investigations in which locomotor activity of animals was reduced by this and other related compounds (Millichap et.al., 1968).

Gross and Wilson (1964), in a report of ten case studies of medication effects on behavioral outcomes and EEG profiles, determined that some of the amphetamines were useful and that phenobarbital often made the patient worse, but that diphenylhydantoin was rather effective. In fact, these medications were found to be less effective than placebo administrations.

Captodiamine hydrochloride has been reported to be effective in organic brain disorders (Low & Myers, 1958). Forty hyperkinetic children with patterns of organic brain damage were treated with varying doses (lo-250 mg. daily) of this drug for a period ranging from 3 to 17 months. Striking improvement in behavior with no significant toxic reactions were documented. Conclusions were drawn giving testimony to the value of this drug for the use with hyperkinetic children with brain damage.

CONCLUSION

From our review, drugs seem to have a definite, if circumscribed, role to play in helping children overcome and succeed in spite of their learning handicaps. One reviewer provides an encouraging prospective. "Drugs are obviously not panaceas, though our needs and frustrations may incline us to cast them in this image. New and continual work in psychopharmacology and the physiology of learning allows us to have cautiously optimistic expectations for the future." (Freeman, 1966, p.37).

Several comments can be made that are applicable to the general area of psychopharmacology. As we have learned from this review, most of the available research has dealt with problems that are of a clinical nature. Research regarding the effects of drugs on the learning process is very limited. Freeman (1966) pointed this out after reviewing the research for the past thirty years. Werry and Quay in 1970 also speak to corroborate the need. More studies are needed that employ one or more facets of the learning process as a dependent measure in drug evaluation. Even in those studies using some aspect of the learning process as a dependent measure, it is common to find that the criteria employed is timebound, the task artificial, and occurring in a laboratory situation. Hence

generalizability to the classroom setting is often impaired. Also, much of the available research has used unrepresentative Ss especially in view of the populations to which the experimenters hope to generalize. The choice of Ss in most studies come from adult populations (Alderton & Hoddinott, 1964; Connors & Eisenberg, 1963). Conspicuously scarce in this field are longitudinal studies that attempt to assess long-term effects of a particular drug action. Studies focusing on the synergistic effects of drugs used in combination are also limited. Likewise, so many threats to internal validity make many studies uninterpretable. For example, validity factors of history, maturation, instrumentation, mortality, testing, and regression are often not controlled for.

There are also methodological considerations that are particularly relevant to control for in research dealing specifically with assessing the effects of psychopharmacology. Sprague, et.al. (1970) list three of the common sources of error as:

1. Observer bias.
2. Use of error-prone and/or insensitive measures.
3. Ignoring the necessity for optimal drug dosage; for testing at the height of drug action; and to be sure that medication is both being taken and at the time indicated.

The writer's see reason for optimism in regards to these three sources of error being controlled. A definite, observable trend in this direction of better controlled and more sophisticated studies is appearing and is reflected by the recent research publications in this area.

In summary, it appears that the effect drugs have on intellectual functioning still has to be determined. There was little evidence uncovered in this survey to indicate that the learning process is consistently and reliably affected in certain predictable ways. At this point it might be tentatively concluded that the most effective way to evaluate the drug medicated child psychologically is to be more concerned about his observed and manifest behavioral symptoms and not to depend too completely on expected drug induced changes. It seems highly advisable that the psychologist be aware when a subject is receiving drug medication as well as the drug name and dosage. With this knowledge and the awareness of possible effects and using appropriate clinical skill, the experienced psychologist could serve as a more effective resource for teachers, parents, para-professionals, etc., in assessing individual learning modes that can help provide the best educational placement and provisions.

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APPENDIX

I. Stimulants (Activators)

Amphetamine (Benzedrine)
Dextroamphetamine (dexedrine)
Methamphetamine (Methedrine)
Methylphenidate (Ritalin)
Pipradrol (Meratran)
Iproniezid (Marsilid)
Isocarboxazid (Marplan)
Nialamide (Niamid)
Tranylypromine (Parnate)
Diisopropyl fluorophosphate (DFP)
Eserine
Orphenadrine (Disipal)

II. Tranquilizers (Anti-anxiety - Anti-psychotic)

Azacyclonol (Frenquel)
Benactyzine (Deprol, Suavitil)
Captodiamine (Suvren)
Hydroxyzine (Atarax, Vistaril)
Deserpidine (Harmonyl)
Rescinnamine (Moderil)
Reserpine (Sepasil)
Chlordiazepoxide (Librium)
Chlorpromazine (Thorazine)
Mepazine (Pacatal)
Perphenazine (Trilafon)
Prochlorperazine (Compazine, Stemetil)
Promazine (Sparine)
Promethazine (Phenergan)
Thiopropazate (Dartal)
Thioridazine (Mellaril)
Trifluoperazine (Stelazine)
Triflupromazine (Vesprin)
Meprobamate (Miltown, Equanil)

Appendix (continued)

III. Sedatives (Anticonvulsants)

Phenaglycodol (Ultran)
Butabarbital Sodium (Butisol Sodium)
Pentobarbital Sodium (Nembutal)
Phenobarbital (Luminal)
Secobarbital Sodium (Seconal)
Amobarbital Sodium (Amytal Sodium)
Captodiamine (Suvren, Covatix)
Diphenylhydantoin sodium (Dilantin)
Ectylurea (Nostyn)
Ethchlorvynol (Placidyl)
Glutethimide (Doriden)
Meparfynol (Dormison)
Methyprylon (Noludar)
Oxanamide (Quiactin)
Primidone (Mysoline)